Amendments to the Specification

In the paragraphs below, please add the words shown with an underline, and please delete the words shown with a strikethrough.

Please delete paragraphs [005]-[006] on pages 2-3, and replace them with the following:

-- **[005]** Some methods have been achieved which effectively modulate angiogenesis under certain conditions. For example, AVASTIN ~~Avastin~~® is an anti-VEGF antibody produced by Genentech that is currently in clinical trials for treatment of breast cancer, colorectal cancer, small cell lung cancer, and renal cancer, and that has been shown to have an anti-angiogenic effect on certain tumor types. AVASTIN ~~Avastin~~® has received FDA approval for use in patients having a colorectal cancer that has disseminated. Similarly, MACUGEN ~~Macugen~~® is an aptamer from Eyetech/Pfizer that targets VEGF and that has a demonstrated anti-angiogenic effect with regard to macular degeneration (Eyetech Study Group, 2003, Ophthalmology 110(5):979-86).

[006] To date, various polypeptides have been described that stimulate angiogenesis (e.g. VEGFs, FGFs, PDGFB, EGF, LPA, HGF, PD-ECF, IL-8, angiogenin, TNF-alpha, TGF-beta, TGF-alpha, proliferin, and PLGF) or inhibit angiogenesis (e.g. ENDOSTATIN ~~Endostatin~~®, ANGIOSTATIN ~~Angiostatin~~®, and thrombospondin). Although some methods have been achieved which effectively modulate angiogenesis in certain situations, clearly more therapeutics are needed to treat a broader range of diseases and conditions, as well as to increase the efficacy of the methods that already exist. Therefore, what is needed in the art are new compositions and methods for modulating angiogenesis to inhibit the undesired growth of blood vessels associated with certain diseases and conditions. What is also needed are methods and compositions for modulating tumorigenesis and/or permeability of a tumor. What is further needed are new methods for promoting angiogenesis in patients suffering from diseases or conditions that are indicated by decreased vascularization. Moreover, what is also needed are methods for identifying therapeutic agents capable of modulating angiogenesis effectively and safely in a patient. --

Please delete paragraph [098] on pages 30-31, and replace it with the following:

--**[098]** AFFI-GEL ~~Affi-gel~~ blue beads (Bio-Rad, 50-75 μm diameter) were soaked in a solution of apelin peptide (0.1 mg/ml), mutated apelin peptide (0.25 mg/ml), BSA (Sigma, 1 mg/ml), or rm VEGF-164 (R&D Systems, 0.25 mg/ml) for 1 hour on ice. Beads were microsurgically implanted in an avascular region, the posterior lateral mesoderm, of stage 24-26 embryos. Embryos were cultured in 0.2X MMR until stage 35-37, at which time they were prepared for whole mount *in situ* hybridization analysis as described in Example 2. The embryonic vascular system was visualized using an antisense probe directed against transcripts encoding the Xenopus vascular marker, erg (Baltzinger et al., 1999, Dev. Dyn. 216:420-33). --

Please delete paragraph [0102] on pages 31-32, and replace it with the following:

--**[0102]** Bovine aortic endothelial cells (BAE) were cultured in DMEM supplemented with 10% fetal bovine serum (FBS) and penicillin/streptomycin. For generation of stable cell lines expressing APJ, the mouse APJ coding region was cloned into the pcDNA 3.1 vector downstream of the CMV promoter, in frame with a myc epitope at the C-terminal end of the protein, and upstream of the neomycin gene. Bovine aortic endothelial (BAE) cells were transfected with this construction using the SUPERFECT ~~Superfect~~ transfection kit (Qiagen) and selected for resistance to G418 (600 μg/ml). Colonies were isolated and screened using RT-PCR for expression of mouse APJ and also by immunocytochemistry for expression of the myc epitope. A total of 14 clones were found to express mouse APJ, and one of these (BAE/APJ#2) was used for both the proliferation and migration assays. --

Please delete paragraph [0113] on pages 34, and replace it with the following:

--**[0113]** A dot blot membrane carrying cDNA prepared from 154 human tumors was obtained from BD Biosciences (San Jose, CA). Each tumor sample was accompanied by an adjacent non-tumor tissue from the same individual. An approximately 2 kb fragment of the human apelin sequence was labeled with ^{32}P by the Random Priming method, using a standard protocol (Feinberg and Vogelstein, 1984). The ^{32}P-labeled probe was hybridized overnight with the dot blot membrane in a hybridization solution provided by BD with the membrane (BD

EXPRESSHYB ~~ExpressHyb™~~ Hybridization solution). After hybridization, the membrane was washed with prewarmed Wash Solution I (2X SSC, 0.5% SDS) for 30 minutes at 68°C, followed by two additional washes for 30 minutes each in Wash Solution I at 68°C. The membrane was then washed two times in prewarmed Wash Solution II (0.2X SSC, 0.5% SDS) for 30 minutes each at 68°C. The membrane was then wrapped in plastic wrap and exposed to X-ray film, in the presence of an intensifying screen at –80°C for 17 hours. Apelin expression was increased in approximately one third of the 154 tumor samples, relative to adjacent non-tumor tissue (58 out of 154 samples)(Figure 10A). --